2. (Amended) A composition for the percutaneous administration of an opioid analgesic which comprises a therapeutic amount of the opioid analgesic in association with a vehicle for providing a transdermal flux of the opioid analgesic when applied to a human body surface or membrane, a quantity of a distressing substance and a membrane which is permeable to the opioid analgesic and non-permeable to the distressing substance, said distressing substance not penetrating the skin of a human patient when the composition is applied to the skin of said patient and said distressing substance when ingested orally or as parenteral bolus injection together with the opioid analgesic will produce a distressful reaction in the recipient.

B1 Contd

3. (Amended) A composition according to claim 1 , wherein the distressing substance is selected from the group consisting of emetics, nauseants and flavouring substances.

4. (Amended) A composition according to claim 2, wherein the distressing substance is selected from the group consisting of ergolides, quatenary ammonium compounds, opioid antagonists, emetics, and atropine or salts thereof.

5. (Amended) A composition according to claim 1, wherein the distressing substance is incorporated in a vehicle being the same vehicle as for the opioid analgesic.

Please **add** the following new claims:

B2

16. (New) A composition according to claim 2, wherein the distressing substance is incorporated in a vehicle being the same vehicle as for the opioid analgesic.

17. (New) A composition for the percutaneous administration of an opioid analgesic which comprises a therapeutic amount of the opioid analgesic in association with a vehicle for providing a transdermal flux of the opioid analgesic when applied to a human body surface or membrane, and a quantity of a distressing substance selected from the group consisting of ergolides, quaternary

B2 Cont

ammonium compounds, atropine or salts thereof, and mixtures thereof, said distressing substance separated from the opioid analgesic and not penetrating the skin of a human patient when the composition is applied to the skin of said patient, said distressing substance when ingested orally or as parenteral bolus injection together with the opioid analgesic will produce a distressful reaction in the recipient.

I. Status of the Claims

Claims 1-15 are pending and claims 1-5 have been amended. Support for the amendments can be found throughout the specification, e.g. the originally filed claims. It is respectfully submitted that no new matter has been added by virtue of the present amendment.

II. Rejections Under 35 U.S.C. §103

In the Office Action, claims 1-15 were rejected under 35 U.S.C. §103 (a) on the grounds of being obvious over U.S. Patent No. 5,474,783 to Miranda, et al (the Miranda patent). The Examiner states that "[o]ne of skill in the art would have been motivated to follow the suggestions of Miranda to combine the possible agents (atropine and buprenorphine) in order to fight a wider range of ailments" and that "[a] skilled artisan also would have been motivated to follow the suggestion in the art to include a penetration enhancer in order to better transmit the active agents across into the skin." The Examiner concludes that "[i]t would have been obvious to one of ordinary skill in the art, at the time of the invention to follow the suggestions of Miranda with an expected result of a composition comprising atropine, buprenorphine, a penetration enhancer and a device to transit it into the skin."

Before addressing the rejection, a brief review of the present invention is in order. The present invention, as presently claimed, is directed to a transdermal composition comprising an opioid analgesic in association with a vehicle for providing a transdermal flux of the opioid analgesic when applied to a human body surface or membrane and a quantity of a distressing substance which does not penetrate the skin of a human patient when the composition is applied to the skin of the patient. Thus, when the composition is used as directed, the distressing substance will not permeate

through the skin of the user and therefore will not provide a physiological effect. If, however, an abuser attempts to orally or parenterally administer the content of the transdermal composition, the distressing agent will cause distress to the user and therefore may deter attempts of abuse.

Initially, it is respectfully submitted that the Miranda patent does not teach or suggest a composition comprising buprenorphine and atropine. The Miranda patent does list atropine and buprenorphine in an exhaustive list (from column 10, line 48 to column 12, line 33) of possible agents that can be included in the dosage forms described therein. However, the Miranda patent does not teach or suggest to one skilled in the art to pick and choose these two particular agents from the plethora of possible combinations from the list of active agents in this reference.

Further, even assuming arguendo that Miranda does teach a composition comprising buprenorphine and atropine, the reference does not teach or suggest a distressing substance not penetrating the skin of a human patient when the composition is applied to the skin of the patient, as recited in the present claims. The Miranda patent describes transdermal compositions which are intended to allow the drug(s) included therein to permeate through the skin in order to provide a pharmacological response. This reference does not teach or suggest incorporating an agent into a transdermal composition wherein the drug does not permeate through the skin upon application as recited in the present claims.

In view of the actions taken and arguments presented, the Examiner is respectfully requested to remove the rejections under 35 U.S.C. §103.

III. Conclusion

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached pages are captioned "**Version With Markings To Show Changes Made**."

It is now believed that the above-referenced rejections have been obviated and it is respectfully requested that they be withdrawn. It is believed that all claims are now in condition for allowance.

According to currently recommended Patent Office policy the Examiner is respectfully requested to contact the undersigned in the event that a telephonic interview will advance the prosecution of this application.

An early and favorable action is earnestly solicited.

Respectfully submitted,
DAVIDSON, DAVIDSON & KAPPEL, LLC

By: _____
Robert J. Paradiso
Reg. No. 41,240

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue, 14th Floor
New York, New York 10018
(212) 736-1940